

(19) United States

(12) Patent Application Publication (10) Pub. No.: US 2021/0279870 A1 Barnes et al.

(43) **Pub. Date:** Sep. 9, 2021

(54) METHODS, SYSTEMS, AND APPARATUSES FOR QUANTITATIVE ANALYSIS OF HETEROGENEOUS BIOMARKER DISTRIBUTION

(71) Applicants: Ventana Medical Systems, Inc., Tucson, AZ (US); OREGON HEALTH & SCIENCE UNIVERSITY, Portland, OR (US)

(72) Inventors: Michael Barnes, Oro Valley, AZ (US); David Chafin, Tucson, AZ (US); Karl Garsha, Sahuarita, AZ (US); Thomas M. Grogan, Tucson, AZ (US); Esteban Roberts, Tucson, AZ (US); Benjamin Stevens, Oro Valley, AZ (US); Franklin Ventura, Tucson, AZ (US); Christophe Chefd'hotel, Sunnyvale, CA (US); Kandavel Shanmugam, Chandler, AZ (US); Joe Gray, Lake Oswego, OR (US); Damien Ramunno-Johnson, Vancouver, WA (US); Tothu Tania Vu, Portland, OR (US); Brian J. Druker, Portland, OR (US); Thomas Jacob, Beaverton, OR (US)

(21) Appl. No.: 17/329,966

(22) Filed: May 25, 2021

Related U.S. Application Data

Continuation of application No. 16/811,688, filed on Mar. 6, 2020, now Pat. No. 11,049,247, which is a continuation of application No. 15/606,122, filed on May 26, 2017, now Pat. No. 10,664,967, which is a continuation of application No. PCT/EP2015/ 078532, filed on Dec. 3, 2015.

Provisional application No. 62/086,840, filed on Dec. 3, 2014.

Publication Classification

| (51) | Int. Cl. | |
|------|-----------|-----------|
| | G06T 7/00 | (2006.01) |
| | G06T 7/11 | (2006.01) |
| | G06K 9/00 | (2006.01) |
| | G06T 7/90 | (2006.01) |

(52) U.S. Cl.

CPC G06T 7/0012 (2013.01); G06T 7/11 (2017.01); G06K 9/00147 (2013.01); G06T 7/90 (2017.01); G06K 9/6222 (2013.01); G06T 2207/20104 (2013.01); G06T 2207/30024 (2013.01); G06T 2207/30096 (2013.01); G06T 2207/20152 (2013.01); G06T 2207/10056 (2013.01)

(57)**ABSTRACT**

Methods, systems, and apparatuses for detecting and describing heterogeneity in a cell sample are disclosed herein. A plurality of fields of view (FOV) are generated for one or more areas of interest (AOI) within an image of the cell sample are generated. Hyperspectral or multispectral data from each FOV is organized into an image stack containing one or more z-layers, with each z-layer containing intensity data for a single marker at each pixel in the FOV. A cluster analysis is applied to the image stacks, wherein the clustering algorithm groups pixels having a similar ratio of detectable marker intensity across layers of the z-axis, thereby generating a plurality of clusters having similar expression patterns.

